

SEQUENCE LISTING

<110> Lavie, Arnon
Konrad, Manfred
Ravandi, Farhad

<120> Use of Specifically Engineered Enzymes to Enhance the Efficacy of Prodrugs

<130> 02-134-D

<160> 5

<170> PatentIn version 3.0

<210> 1

<211> 260

<212> PRT

<213> Homo sapiens

<400> 1

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Met Ala Thr Pro Pro Lys Arg Ser Cys Pro Ser Phe Ser Ala Ser Ser
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Glu Gly Thr Arg Ile Lys Lys Ile Ser Ile Glu Gly Asn Ile Ala Ala
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Gly Lys Ser Thr Phe Val Asn Ile Leu Lys Gln Leu Cys Glu Asp Trp
35        40        45

Glu Val Val Pro Glu Pro Val Ala Arg Trp Cys Asn Val Gln Ser Thr
50        55        60

Gln Asp Glu Phe Glu Glu Leu Thr Met Ser Gln Lys Asn Gly Gly Asn
65        70        75        80

Val Leu Gln Met Met Tyr Glu Lys Pro Glu Arg Trp Ser Phe Thr Phe
85        90        95

Gln Thr Tyr Ala Cys Leu Ser Arg Ile Arg Ala Gln Leu Ala Ser Leu
100       105       110

Asn Gly Lys Leu Lys Asp Ala Glu Lys Pro Val Leu Phe Phe Glu Arg
115       120       125

Ser Val Tyr Ser Asp Arg Tyr Ile Phe Ala Ser Asn Leu Tyr Glu Ser
130       135       140

Glu Cys Met Asn Glu Thr Glu Trp Thr Ile Tyr Gln Asp Trp His Asp
145       150       155       160

Trp Met Asn Asn Gln Phe Gly Gln Ser Leu Glu Leu Asp Gly Ile Ile
165       170       175

Tyr Leu Gln Ala Thr Pro Glu Thr Cys Leu His Arg Ile Tyr Leu Arg
180       185       190

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Gly Arg Asn Glu Glu Gln Gly Ile Pro Leu Glu Tyr Leu Glu Lys Leu
 195 200 205

His Tyr Lys His Glu Ser Trp Leu Leu His Arg Thr Leu Lys Thr Asn
 210 215 220

Phe Asp Tyr Leu Gln Glu Val Pro Ile Leu Thr Leu Asp Val Asn Glu
 225 230 235 240

Asp Phe Lys Asp Lys Tyr Glu Ser Leu Val Glu Lys Val Lys Glu Phe
 245 250 255

Leu Ser Thr Leu
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<210> 2
 <211> 277
 <212> PRT
 <213> Homo sapiens

<400> 2

Met Ala Ala Gly Arg Leu Phe Leu Ser Arg Leu Arg Ala Pro Phe Ser
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Ser Met Ala Lys Ser Pro Leu Glu Gly Val Ser Ser Ser Arg Gly Leu
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His Ala Gly Arg Gly Pro Arg Arg Leu Ser Ile Glu Gly Asn Ile Ala
 35 40 45

Val Gly Lys Ser Thr Phe Val Lys Leu Leu Thr Lys Thr Tyr Pro Glu
 50 55 60

Trp His Val Ala Thr Glu Pro Val Ala Thr Trp Gln Asn Ile Gln Ala
 65 70 75 80

Ala Gly Asn Gln Lys Ala Cys Thr Ala Gln Ser Leu Gly Asn Leu Leu
 85 90 95

Asp Met Met Tyr Arg Glu Pro Ala Arg Trp Ser Tyr Thr Phe Gln Thr
 100 105 110

Phe Ser Phe Leu Ser Arg Leu Lys Val Gln Leu Glu Pro Phe Pro Glu
 115 120 125

Lys Leu Leu Gln Ala Arg Lys Pro Val Gln Ile Phe Glu Arg Ser Val
 130 135 140

Tyr Ser Asp Arg Tyr Ile Phe Ala Lys Asn Leu Phe Glu Asn Gly Ser
 145 150 155 160

Leu Ser Asp Ile Glu Trp His Ile Tyr Gln Asp Trp His Ser Phe Leu
 165 170 175

Leu Trp Glu Phe Ala Ser Arg Ile Thr Leu His Gly Phe Ile Tyr Leu
 180 185 190

Gln Ala Ser Pro Gln Val Cys Leu Lys Arg Leu Tyr Gln Arg Ala Arg
 195 200 205

Glu Glu Glu Lys Gly Ile Glu Leu Ala Tyr Leu Glu Gln Leu His Gly
 210 215 220

Gln His Glu Ala Trp Leu Ile His Lys Thr Thr Lys Leu His Phe Glu
 225 230 235 240

Ala Leu Met Asn Ile Pro Val Leu Val Leu Asp Val Asn Asp Asp Phe
 245 250 255

Ser Glu Glu Val Thr Lys Gln Glu Asp Leu Met Arg Glu Val Asn Thr
 260 265 270

Phe Val Lys Asn Leu
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<210> 3
 <211> 250
 <212> PRT
 <213> Drosophila

<400> 3

Met Ala Glu Ala Ala Ser Cys Ala Arg Lys Gly Thr Lys Tyr Ala Glu
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Gly Thr Gln Pro Phe Thr Val Leu Ile Glu Gly Asn Ile Gly Ser Gly
 20 25 30

Lys Thr Thr Tyr Leu Asn His Phe Glu Lys Tyr Lys Asn Asp Ile Cys
 35 40 45

Leu Leu Thr Glu Pro Val Glu Lys Trp Arg Asn Val Asn Gly Val Asn
 50 55 60

Leu Leu Glu Leu Met Tyr Lys Asp Pro Lys Lys Trp Ala Met Pro Phe
 65 70 75 80

Gln Ser Tyr Val Thr Leu Thr Met Leu Gln Ser His Thr Ala Pro Thr
 85 90 95

Asn Lys Lys Leu Lys Ile Met Glu Arg Ser Ile Phe Ser Ala Arg Tyr
 100 105 110

Cys Phe Val Glu Asn Met Arg Arg Asn Gly Ser Leu Glu Gln Gly Met
 115 120 125

Tyr Asn Thr Leu Glu Glu Trp Tyr Lys Phe Ile Glu Glu Ser Ile His
 130 135 140

Val Gln Ala Asp Leu Ile Ile Tyr Leu Arg Thr Ser Pro Glu Val Ala
 145 150 155 160

Tyr Glu Arg Ile Arg Gln Arg Ala Arg Ser Glu Glu Ser Cys Val Pro

165										170					175				
Leu	Lys	Tyr	Leu	Gln	Glu	Leu	His	Glu	Leu	His	Glu	Asp	Trp	Leu	Ile				
			180						185				190						
His	Gln	Arg	Arg	Pro	Gln	Ser	Cys	Lys	Val	Leu	Val	Leu	Asp	Ala	Asp				
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Leu	Asn	Leu	Glu	Asn	Ile	Gly	Thr	Glu	Tyr	Gln	Arg	Ser	Glu	Ser	Ser				
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Ile	Phe	Asp	Ala	Ile	Ser	Ser	Asn	Gln	Gln	Pro	Ser	Pro	Val	Leu	Val				
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<211> 232																			
<212> PRT																			
<213> Homo sapiens																			
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Val	Gln	Arg	Tyr	Ala	Trp	Pro	Pro	Asp	Lys	Glu	Gln	Glu	Lys	Glu	Lys				
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Lys	Ser	Val	Ile	Cys	Val	Glu	Gly	Asn	Ile	Ala	Ser	Gly	Lys	Thr	Thr				
			20					25					30						
Cys	Leu	Glu	Phe	Phe	Ser	Asn	Ala	Thr	Asp	Val	Glu	Val	Leu	Thr	Glu				
		35					40					45							
Pro	Val	Ser	Lys	Trp	Arg	Asn	Val	Arg	Gly	His	Asn	Pro	Leu	Gly	Leu				
	50					55					60								
Met	Tyr	His	Asp	Ala	Ser	Arg	Trp	Gly	Leu	Thr	Leu	Gln	Thr	Tyr	Val				
65					70				75					80					
Gln	Leu	Thr	Met	Leu	Asp	Arg	His	Thr	Arg	Pro	Gln	Val	Ser	Ser	Val				
			85					90					95						
Arg	Leu	Met	Glu	Arg	Ser	Ile	His	Ser	Ala	Arg	Tyr	Ile	Phe	Val	Glu				
		100						105					110						
Asn	Leu	Tyr	Arg	Ser	Gly	Lys	Met	Pro	Glu	Val	Asp	Tyr	Val	Val	Leu				
	115						120					125							
Ser	Glu	Trp	Phe	Asp	Trp	Ile	Leu	Arg	Asn	Met	Asp	Val	Ser	Val	Asp				
	130					135					140								
Leu	Ile	Val	Tyr	Leu	Arg	Thr	Asn	Pro	Glu	Thr	Cys	Tyr	Gln	Arg	Leu				
145					150					155					160				
Lys	Lys	Arg	Cys	Arg	Glu	Glu	Glu	Lys	Val	Ile	Pro	Leu	Glu	Tyr	Leu				
			165						170					175					

Glu Ala Ile His His Leu His Glu Glu Trp Leu Ile Lys Gly Ser Leu
 180 185 190

Phe Pro Met Ala Ala Pro Val Leu Val Ile Glu Ala Asp His His Met
 195 200 205

Glu Arg Met Leu Glu Leu Phe Glu Gln Asn Arg Asp Arg Ile Leu Thr
 210 215 220

Pro Glu Asn Arg Lys His Cys Pro
 225 230

<210> 5
 <211> 260
 <212> PRT
 <213> Artificial

<220>
 <223> Modified deoxycytidine kinase

<400> 5

Met Ala Thr Pro Pro Lys Arg Ser Cys Pro Ser Phe Ser Ala Ser Ser
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Glu Gly Thr Arg Ile Lys Lys Ile Ser Ile Glu Gly Asn Ile Ala Ala
 20 25 30

Gly Lys Ser Thr Phe Val Asn Ile Leu Lys Gln Leu Cys Glu Asp Trp
 35 40 45

Glu Val Val Pro Glu Pro Val Ala Arg Trp Cys Asn Val Gln Ser Thr
 50 55 60

Gln Asp Glu Phe Glu Glu Leu Thr Met Ser Gln Lys Asn Gly Gly Asn
 65 70 75 80

Val Leu Gln Met Met Tyr Glu Lys Pro Glu Arg Trp Ser Phe Thr Phe
 85 90 95

Gln Thr Tyr Val Cys Leu Ser Met Ile Arg Ala Gln Leu Ala Ser Leu
 100 105 110

Asn Gly Lys Leu Lys Asp Ala Glu Lys Pro Val Leu Phe Phe Glu Arg
 115 120 125

Ser Val Tyr Ser Ala Arg Tyr Ile Phe Ala Ser Asn Leu Tyr Glu Ser
 130 135 140

Glu Cys Met Asn Glu Thr Glu Trp Thr Ile Tyr Gln Asp Trp His Asp
 145 150 155 160

Trp Met Asn Asn Gln Phe Gly Gln Ser Leu Glu Leu Asp Gly Ile Ile
 165 170 175

Tyr Leu Gln Ala Thr Pro Glu Thr Cys Leu His Arg Ile Tyr Leu Arg
 180 185 190

Gly Arg Asn Glu Glu Gln Gly Ile Pro Leu Glu Tyr Leu Glu Lys Leu
195 200 205

His Tyr Lys His Glu Ser Trp Leu Leu His Arg Thr Leu Lys Thr Asn
210 215 220

Phe Asp Tyr Leu Gln Glu Val Pro Ile Leu Thr Leu Asp Val Asn Glu
225 230 235 240

Asp Phe Lys Asp Lys Tyr Glu Ser Leu Val Glu Lys Val Lys Glu Phe
245 250 255

Leu Ser Thr Leu
260